**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

| | | |
|---|---|---|
| SCIELE PHARMA, INC., et al., | ) | |
| | ) | |
| Plaintiffs, | ) | |
| | ) | |
| v. | ) | C.A. NO. 09-037 (RBK) (JS) |
| | ) | |
| LUPIN LTD., et al., | ) | (CONSOLIDATED) |
| | ) | |
| Defendants. | ) | |
| SHIONOGI INC., et al., | ) | |
| | ) | |
| Plaintiffs, | ) | |
| | ) | |
| v. | ) | C.A. NO. 10-135 (RBK) (JS) |
| | ) | |
| MYLAN INC., et al., | ) | **HIGHLY CONFIDENTIAL** |
| | ) | **FILED UNDER SEAL** |
| Defendants. | ) | |
| | ) | |

**THE LUPIN DEFENDANTS' ANSWERING BRIEF IN OPPOSITION TO PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTION AND RECALL**

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# TABLE OF CONTENTS

# TABLE OF AUTHORITIES

**Page**

**Cases**

**Federal Statutes**



**Federal Regulations**

## I. NATURE AND STAGE OF PROCEEDINGS

Three months after receiving final approval from the Food and Drug Administration to market its generic Fortamet® ANDA product, [redacted], and two days after it publicly announced that it would market its product, Lupin launched its ANDA product onto the U.S. market on September 30, 2011. Almost two weeks later, pursuant to a month-long briefing schedule requested by Shionogi, Shionogi seeks the exceptional relief of an injunction barring Lupin from further sales and the even more extraordinary relief of a recall of the product already in the marketplace.

Although stating that Lupin's product infringes two valid patents, Shionogi does not even try to argue in support of its motion for exceptional relief that its '859 patent is infringed. Its contention that the '866 patent is infringed relies solely on a statement in Lupin's product labeling, a statement FDA rules required to be copied from plaintiff's Fortamet® label and which is inconsistent with the actual test data on Lupin's product that uniformly show no infringement.

Shionogi also ignores the fact that the '866 patent is invalid; an apparent PTO error in the printed patent means that claims which Shionogi asserts against Lupin were actually disallowed by the PTO examiner as obvious over the prior art. The exceptional relief of an injunction should not be granted for claimed infringement of patent claims issued by mistake.

## II. SUMMARY OF ARGUMENT

All four preliminary injunction factors require denial of a preliminary injunction.

### A. No Likelihood of Success On The Merits

Plaintiffs' infringement claim is disproved by unrebutted evidence. The key question of infringement is whether a *single dose* of Lupin's ANDA product administered following dinner produces a $T_{max}$ from *5.5 - 7.5* hours. The only test of *Lupin's* product in the record shows that a single dose of Lupin's product following dinner gives a $T_{max}$ of [redacted], which demonstrates

*non*-infringement. Plaintiffs seize upon Lupin's labeling as an admission that trumps the evidence, because that labeling reports a $T_{max}$ of 6 hours. However, per FDA regulations, the labeling of Lupin's product merely reports the result of a multi-dose test on plaintiffs' Fortamet® product, not on Lupin's product.

Plaintiffs' position concerning the validity of the '866 patent claims presumes that the claims of the patent were found patentable by the examiner and thus the patent should be presumed valid. As described below in plaintiffs' own words, however, the examiner was unwilling to give plaintiffs claims up to a $T_{max}$ of 7.5 hours in view of prior art teaching a $T_{max}$ of 8 hours. Only through an apparent error in the PTO were plaintiffs able to obtain the claims being sued upon here, and thus the presumption of validity should not apply. Moreover, on the substance, plaintiffs ignore an important change in the law since the patent was issued, which leads strongly to the conclusion that these patent claims are indeed invalid.

**B. No Irreparable Injury Will Be Remedied By A Preliminary Injunction**

Despite its speculative claims, Shionogi will not be irreparably harmed if this case proceeds to the merits without extraordinary relief. Shionogi already is competing with a number of similar generic metformin extended release products. [redacted]

The declining sales will contribute a decreasing amount to Shionogi's net profits, [redacted]

Shionogi itself has prepared projections showing its predicted loss from competition with Lupin, demonstrating that its harm is predictable and quantifiable and that, as is the norm even in patent cases, money damages will suffice to compensate it, should a factfinder conclude that Lupin's

product infringes a valid patent. This may explain why Shionogi delayed in seeking injunctive relief and took no steps to protect itself from a launch of Lupin's product, despite clear indications since the summer that Lupin was planning to sell its ANDA product this year.

**C. The Balance of Hardships Favors Denial Of The Motion**

In this unusual situation where not only is the brand market declining [redacted] Lupin is the one which will be irredeemably harmed if it is forced to stop selling now. If Lupin must wait for a year or more to enter the market, it may find that the market no longer exists. Added to this real threat is Lupin's loss of its 180 day exclusivity if it is enjoined, its right to benefit from having filed its ANDA one year before the next generic competitor, and the harm to its reputation and relationship with its customers.

**D. The Public Interest In Favor Of Access To Generic Drugs Supports Denial Of The Motion**

Congress has determined that, in the ordinary course, a generic drug should be available to the public 30 months after the patent owner has been notified of the generic drug application, unless the patent has been adjudged valid and infringed in the interim. While the public interest in protecting valid patent rights can in some cases represent an offsetting public interest, that situation does not apply here because the plaintiff is suing on patent claims that the PTO examiner disallowed as obvious but were issued through PTO error. There has been no attempt to correct the patent, and thus the only public interest at stake here calls for denial of the motion.

## III. STATEMENT OF FACTS

Lupin Limited is among the top five pharmaceutical companies in India and is ranked fifth by prescriptions in the United States. For the fiscal year ended March 2011, its revenues and profit after tax were US$ 1.3 billion and US$ 193 million respectively. Its worldwide

manufacturing facilities are approved by international regulatory agencies including the U.S. FDA. Through its sales and marketing headquarters in Baltimore, MD, its United States subsidiary Lupin Pharmaceuticals, Inc. delivers generic medicines to U.S. consumers. One of those medicines is a generic version of Fortamet®.

Fortamet® is indicated as an adjunct (to diet and exercise) to lower blood glucose to improve glycemic control in adults with Type 2 diabetes. Its active ingredient, metformin, has been known and used for years. Thus, the market in which Fortamet® competes is highly saturated, including numerous generic extended-release metformin products, immediate release metformin products, and several branded products as well as numerous other oral treatments for Type 2 diabetes. Gleason/Hofmann Dec. at 15; Exh. 1 of the Declaration of Stephen B. Brauerman ("Brauerman Dec.") [redacted]. Fortamet® is available in two dosage forms: 500mg and 1000mg. [redacted] Sales of the 1000 mg dosage form have also been declining over the past three years [redacted] Hoffman Dec. at 15; Gleason/Hofmann Dec. at 31.

Lupin's Abbreviated New Drug Application (ANDA) for a generic version of Fortamet® uses the same active therapeutic ingredient (metformin), but the design of the two products is substantially different. Among the requirements for approval by the FDA of an ANDA is a showing that the generic drug is bioequivalent to the brand drug. 21 U.S.C. § 355(j)(2)(A)(iv). In determining whether a generic drug like Lupin's is bioequivalent to the "reference listed drug", *i.e.*, Fortamet®, the FDA looks at two pharmacokinetic parameters. One parameter is the "maximum or peak drug concentration" ($C_{max}$) in the blood or plasma, which measures rate of absorption. The other parameter is "Area Under the plasma concentration Curve (AUC), which

measures the extent of absorption. These two – $C_{max}$ and AUC – are the "parameters of interest according to FDA."[1] FDA has determined that up to a 20% variation in these parameters is acceptable, a determination that was explicitly based on the agency's access to scientific expertise.[2]

Instead, per FDA regulations requiring that the generic drug's labeling be the same as that of the brand drug, the labeling for Lupin's product includes a table reporting data from a different test on the *Fortamet*® product that is taken verbatim from the Fortamet® label (other than changing the product name, per FDA rules, from Fortamet® to "Extended-Release Metformin"):

[1] *See* Approved Drug Products With Therapeutic Equivalence Evaluations, published in 2011 by FDA (31st edition) at pages viii-ix. This publication is commonly referenced to as the "Orange Book" (the cover of the hard copy of this publication was traditionally orange). Brauerman Dec. Exh. 3.

[2] *Id.* at page ix.

| **Pharmacokinetic Parameters (mean ± SD)** | **Extended – Release Metformin 2000 mg (administered q.d. after dinner)** | **Immediate-Release Metformin 2000 mg (1000 mg b.i.d.)** |
|---|---|---|
| $AUC_{0\text{-}24\ hr}$ (ng·hr/mL) | 26,811 ± 7055 | 27,371 ± 5,781 |
| $T_{max}$ (hr) | 6 (3-10) | 3 (1-8) |
| $C_{max}$ (ng/mL) | 2849 ± 797 | 1820 ± 370 |

Brauerman Dec. Exh. 4.

[redacted] Fortamet® sales are only two percent of the revenues of the Japanese parent Shionogi and Company, Ltd. ("Shionogi Japan"). Gleason/Hofmann Dec. at 32. Because it is a mature product for a chronic indication [redacted] Fortamet® continues to contribute to Shionogi's profits for the time being. [redacted]

Gleason/Hofmann Dec. at ¶ 31.

On December 3, 2008, Lupin notified Watson and Andrx that it had filed ANDA No. 90-692 with the FDA to manufacture and sell a generic version of Fortamet®. Lupin's filing with the FDA included a paragraph IV certification that claims the '859 and '866 patents are invalid, unenforceable, and/or will not be infringed by the manufacture, use, offer for sale, or sale of Lupin's ANDA products. On January 15, 2009, Sciele (now Shionogi) filed a patent infringement suit against Lupin, which resulted in a thirty-month stay of the FDA's approval of Lupin's ANDA.

On April 20, 2011, the FDA gave its tentative approval of Lupin's ANDA, and on June 29, 2011 the FDA formally approved Lupin's ANDA, as the thirty-month stay had expired. Gleason/Hofmann Dec. at 19; Brauerman Dec. Exh. 5). [redacted]

[redacted] In June, the Wall Street Journal published a statement from a Lupin spokesman that Lupin intended to launch its generic Fortamet® "this year"; on September 28, 2011, the Wall Street Journal published another announcement that Lupin intended to market its generic Fortamet® soon. Brauerman Dec. Exhs. 8-9. [redacted] Shionogi did not ask Lupin for notice before it intended to launch, and took no steps to protect itself from Lupin marketing its ANDA product.

Two days after learning of Lupin's launch, Shionogi approached Lupin's counsel to ask for confirmation that Lupin was considering a launch, and asked for a response the next day. Noyes Dec. at Exh. 8. When Lupin's counsel confirmed the launch, Noyes Dec. at Exh. 8, Shionogi still waited before seeking injunctive relief, ultimately asking the Court for a briefing schedule over the course of one month. [redacted]

[redacted]

## IV. ARGUMENT

### A. Plaintiffs Have Not Established A Likelihood Of Success On The Merits

#### 1. Legal Standard

A preliminary injunction in Hatch-Waxman pharmaceutical cases is a "drastic and extraordinary remedy that is not to be routinely granted." *King Pharms. Inc. v. Sandoz, Inc.*, C.A. No. 08-5974, 2010 WL 1957640, at *1 (D.N.J. May 17, 2010) (Brown, Ch. J.) (not for publication); *EMSL Analytical, Inc. v. Testamerica Analytical Testing Corp.,* Civ. No. 05-5259, 2006 WL 892718, at *2 (D.N.J. April 4, 2006).

Consistent with equitable principles, the patentee must establish four separate factors: (1) reasonable likelihood of the movant's success on the merits; (2) irreparable harm if an injunction is not granted; (3) the balance of hardships between the parties; and (4) the public interest. *See*, *e.g.*, *Winter v. NRDC, Inc.*, 555 U.S. 7, 20 (2008); *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 391 (2006); *Altana Pharma AG v. Teva Pharm. USA, Inc.*, 566 F.3d 999, 1005 (Fed. Cir. 2009). Plaintiffs "must establish the existence of both [likelihood of success and irreparable injury] to be entitled to a preliminary injunction." *Altana Pharma AG,* 566 F.3d at 1005; *Symbol Technologies, Inc. v. Janam Technologies LLC,* 729 F. Supp. 2d 646, 654 (D. Del. 2010) ("a movant cannot be granted a preliminary injunction unless it establishes *both* of the first two factors, i.e., likelihood of success on the merits and irreparable harm.") (emphasis in original).

This Court must deny a preliminary injunction where the patentee fails to demonstrate a likelihood of success on the merits. As Chief Judge Brown recently explained, "[t]o defeat plaintiffs' [preliminary injunction] motion, [a generic company] need not prove non-

infringement or invalidity; [it] merely needs to 'raise [ ] a substantial question concerning either infringement or invalidity, *i.e.*, assert [ ] an infringement or invalidity defense that [Plaintiffs] cannot prove lacks substantial merit.'" *King Pharms, Inc.,* 2010 WL 1957640, at *1 (quoting *Amazon.com, Inc. v. Barnesandnoble.com, Inc.,* 239 F.3d 1343, 1350-51 (Fed. Cir. 2001).

Plaintiffs incorrectly assert that, to defeat its assertion of likelihood of success on the merits, Lupin must establish that it is "likely to succeed in proving invalidity or unenforceability of the asserted patents." Mem. at 11-12. This is not correct. The burden on the alleged infringer is only to raise a *substantial question* regarding either infringement or validity. *See Altana Pharma AG*, 566 F.3d at 1005-06. "The accused infringer does not face the clear and convincing evidence burden of proof applicable at trial." *Kimberly-Clark Worldwide, Inc. v. First Quality Baby Products, LLC*, 2011 WL 2161072, at * 2 (Fed. Cir. June 1, 2011) (non-precedential) (citing, *e.g.*, *Altana Pharma, AG*, 566 F.3d at 1006), *reh'g and reh'g en banc denied,* 2011 WL 4495619 (2011); *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1372 (Fed. Cir. 2005)).

Plaintiffs assert in a footnote that "there is a debate within the Federal Circuit ... as to whether an alleged infringer can defeat a motion for an injunction by showing a 'substantial question of invalidity,'" citing *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341 (Fed. Cir. 2008) and the precedential dissent from the *Kimberly-Clark* petition for rehearing *en banc*.[3] While there may be debate, the law is that Lupin need only show a substantial question concerning patent infringement or validity.

[3] The author of a dissenting opinion in *Kimberly-Clark*, Judge O'Malley, observed that with respect to the burden adopted by the majority, "District courts across the country have struggled with our precedent in this area, concluding in large measure that, whatever their views of the merits of a particular preliminary injunction request, *this court's precedent virtually mandates denial of all such motions*" (2011 WL 4495619, at * 7) (emphasis added).

**2. A Single Dose Of Lupin's Product Administered Following Dinner [redacted]**

All of the claims asserted against Lupin in this motion[4] depend from Claim 1 of the '866 patent. Claim 1 requires a particular pharmacokinetic profile: "wherein following oral administration of a single dose, the dosage form provides a mean time to maximum plasma concentration ($T_{max}$) of the metformin from 5.5 to 7.5 hours after administration following dinner." Lupin's product does not meet this claim limitation, which forecloses infringement of all claims of the '866 patent.[5]

[redacted]

The Court can safely assume that plaintiffs have no contrary test evidence on Lupin's product showing that a single dose following dinner produces a $T_{max}$ in the 5.5-7.5 hour range.

[4] In a footnote, plaintiffs express an intention to continue to press their assertion that Lupin's product also infringes claim 3 of the '859 patent, even though they are not pursuing that allegation on this motion. There is more than one good reason why plaintiffs would decide not to pursue the '859 patent on this motion, [redacted]

[5] Dependent claims are not infringed if the independent claim on which they depend is not infringed. *Wahpeton Canvas Co. v. Frontier, Inc.,* 870 F.2d 1546, 1552 n. 9 (Fed. Cir. 1989); *see* Markman Op. (D.I. 191) at 15 n. 4.

Judge Schneider previously upheld plaintiffs' claim of work product for tests conducted on Lupin's product D.I. 130 (March 8, 2011). Now in support of their preliminary injunction motion, plaintiffs have chosen to waive work product for favorable tests. *See* the Declaration of Daniel Magiera, PhD (D.I. 211). Presumably if they had favorable $T_{max}$ data on Lupin's products, plaintiffs would have proferred that data now too.

Lacking any evidence of their own to carry their burden of proving infringement, plaintiffs take two tacks. The first is criticizing Lupin's evidence. The second is arguing that Lupin has made an admission that trumps the actual evidence. Neither argument withstands scrutiny.

**a. Lupin's $T_{max}$ Study Is Scientifically Valid Proof of Noninfringement**

Plaintiffs' criticisms of the Lupin study range from the insignificant to the nonsensical. Plaintiffs first say that it is not clear that it was Lupin's ANDA product which was tested. The Declaration of Shirish Kulkarni, the formulator of the Lupin product and filed contemporaneously herewith, disposes of that objection by confirming that it was Lupin's ANDA product that was tested in the after-dinner study.

[redacted]

[6] *See* '866 patent at 16:35-53; 18:31-49; 19:35-36; and 20:49-58, respectively.

[redacted]

[7] [redacted]

[8] During prosecution of the '866 patent, the patent applicant described only one difference between the claimed invention and the dosage form described in the '859 patent -- the '866 patent embodiment had two laser drilled holes rather than one. Brauerman Dec. Exh. 12 at AND 0000236. The patent applicant also represented that the '859 patent's embodiment had a mean $T_{max}$ after dinner 3 hours longer than after breakfast (6.67 hours vs. 9.67 hours). Brauerman Dec. Exh. 12 at AND 0000235-236.

[redacted]

In sum, the only $T_{max}$ study of record where Lupin's product was administered following dinner demonstrates to a 95% confidence level that it gives a $T_{max}$ well *outside* the claimed range of 5.5 - 7.5 hours. Simply stated, Lupin will prove on the merits that its product does not infringe.

**b. Inclusion Of $T_{max}$ Data In Lupin's Package Insert Is Not A Representation Of Infringement**

The distinction between identicality and equivalence is central to the Hatch-Waxman Act. The distinction is also central to understanding why plaintiffs are wrong in their assertion that Lupin has represented that its product gives a $T_{max}$ in the range claimed by the '866 patent.

An application to FDA for approval of a new generic drug must contain "information to show that the active ingredient of the new drug is the same as that of the listed drug." 21 U.S.C. § 355(j)(2)(A)(ii)(I). The new generic drug containing that active ingredient need not be identical to the listed drug, however; the application needs to provide only that the new generic drug is "bioequivalent to the listed drug." 21 U.S.C. § 355(j)(2)(A)(iv). "A drug shall be considered to be bioequivalent to a listed drug if the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses." 21 U.S.C. § 355(j)(8)(B)(i).

The FDA looks at $C_{max}$ to determine rate of absorption and AUC to determine extent of absorption. It is noteworthy that $T_{max}$ is not one of the parameters of interest.[9] Thus Lupin generated a comparison of the $C_{max}$ and AUC values for Fortamet® and Lupin's product, (*see* pages 5-6) which showed that Lupin's product gave bioequivalent, but not identical values as Fortamet®.

Lupin's labeling nonetheless contains none of the $C_{max}$ or AUC (or $T_{max}$ for that matter) data on *Lupin's* product, but instead contains data on the *Fortamet*® product even though the data given to the FDA shows the results are different for the two products. Why does the Lupin labeling contain the data on tests of Fortamet® rather than of Lupin's product? The answer is that FDA regulations mandate that the labeling of a generic drug be the same as that of the reference drug "except for changes *required* . . . because the drug product and the reference listed drug are produced or distributed by different manufacturers." *Zeneca, Inc. v. Shalala*, 213 F.3d 161, 164 (4th Cir. 2000), citing 21 C.F.R. § 314.94(a)(8)(iv) (ellipses are the court's; emphasis added).

Inasmuch as the Fortamet® label contains a table of data, Lupin's label is required to contain that same table. The Supreme Court, after summarizing the statutory scheme, explained the pertinent distinction between the duties of the manufacturer of Fortamet® and of Lupin:

> As a result, brand-name and generic drug manufacturers have different federal drug labeling duties. A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label. A manufacturer seeking

[redacted]

> generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's.

*Pliva, Inc. v. Mensing*, 131 S.Ct. 2567, 2574 (June 23, 2011) *and reh.'g den.,* 180 L. Ed. 2d 924, 2011 WL 3557247 (Aug. 15, 2011) (citations omitted).

This case illustrates the different duties, and these different duties are why Lupin's labeling includes a table of data from a test of plaintiff's product rather than of its own product. Lupin is required to use the Fortamet® data in its labeling, even though the data submitted to FDA shows that the $C_{max}$ and AUC of the Lupin product are not (as stated in Lupin's label) 2849 and 26,811 respectively.[10] The 2849 value for $C_{max}$ and the 26,811 value for AUC was obtained from the Fortamet® package insert, and it is presumably accurate for the Fortamet® product. As the Supreme Court in *Pliva* explained, however, it is not Lupin's responsibility to ensure the accuracy of Lupin's label. Rather, as *Pliva* explained, it is Lupin's duty to ensure that its labeling is the same as that of the reference listed drug (RLD) Fortamet®. This duty holds even if it results in immaterial inaccuracy. *See* 21 C.F.R. § 314.150(a)(2)(iv) (FDA may withdraw approval of an ANDA that "contains any untrue statement of a *material* fact" (emphasis added)). As FDA told the Supreme Court in *Pliva*

> The FDCA requires a manufacturer to show that the labeling proposed for the generic drug is the same as the labeling approved for the RLD. 21 U.S.C. 355(j)(2)(A)(v); see also 21 U.S.C. 355(j)(4)(G). An ANDA therefore must include a comparison of the proposed labeling to the RLD's labeling, 21 C.F.R. 314.94(a)(8)(iv), and a statement that the applicant's proposed labeling * * * is the same as the labeling of the RLD, 21 C.F.R. 314.94(a)(8)(iii); see 21 C.F.R. 314.105(c). This requirement reflects the fundamental premise of the ANDA process that a generic drug can be relied upon as a therapeutic equivalent of its RLD. Accordingly, FDA places a very high priority on assuring consistency in labeling, so as to minimize any cause for confusion among health care

[10] [redacted]

> professionals and consumers as well as to preclude a basis for lack of confidence in the equivalency of generic versus brand name products.[11]

Accordingly, and contrary to plaintiff's argument and the case law upon which it relies,[12] Lupin did not represent in its labeling that its package insert accurately reported the $C_{max}$ of its product as 2849, the AUC of its product as 26,811, or the $T_{max}$ of its product as 6 hours. According to the FDA regulations and statute, Lupin only represented that this test data was reported in the Fortamet® label. Brauerman Dec. Exh. 11 (comparison of Lupin's proposed label with the Fortamet® label presented to the FDA). Lupin also represented, in its ANDA, that the $C_{max}$/AUC figures for the Lupin product and the Fortamet® product were not so different as to preclude a conclusion of bioequivalence. Lupin, however, made no representation that the $T_{max}$ of *its* product following dinner was 6 hours, any more than it represented that the $C_{max}$ of *its* product was 2849 or the AUC of *its* product was 26,811, because Lupin was merely fulfilling its duty to use the same label as the brand drug. *See Pliva,* 131 S. Ct. at 2574-75 (referring to "federal duty of sameness").

The FDA recognizes only "limited" exceptions to this duty of sameness. *See* 54 Fed. Reg. 28884 (July 10, 1989) ("FDA emphasizes that the exceptions to the requirement that a generic drug's labeling be the same as that of the listed drug are limited").[13] This duty required

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[11] Amicus Brief of United States in *Pliva, Inc. v. Mensing*, 2011 WL 741927 at * 3-4 (some citations and internal punctuation omitted; ellipses are in original).

[12] To the extent that the case relied upon by plaintiffs, *Research Foundation of State University of New York v. Mylan Pharms Inc.*, 723 F. Supp. 2d 638, 647 (D. Del. 2010) stands for the proposition that a generic label is a representation that everything in the label is accurate, it is in error at least after *Pliva,* 131 S. Ct. 2567. The same would be said for a case not cited by plaintiff, *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373-74 (Fed. Cir. 2002).

[13] Illustrative exceptions are listed at 54 Fed. Reg. 28884 (middle column), none of which are applicable here.

Lupin to include in its label the table of data from the Fortamet® label, unless a change was required due to the difference in manufacturer. *See* 21 C.F.R. § 314.94(a)(8)(iv).[14]

Here the FDA determined by its approval that no change in label was required, and extreme deference is owed to that expert determination. *Biovail Corp. v. FDA,* 519 F. Supp. 2d 39, 47-48 (D.D.C. 2007) (denying TRO to overturn FDA's determination that a generic company could use same label as reference drug: "Because this determination rests squarely on the FDA's evaluation of scientific data within its area of expertise, it is entitled to a high level of deference from this court.") (internal quotation marks and citations omitted); *see Henley v. FDA*, 77 F.3d 616, 620-21 (2d Cir. 1996) (FDA decision on labeling is owed deference, citing *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir.), *cert. denied*, 516 U.S. 907 (1995)). The FDA's conclusion has support in this record *See* Shepherd Dec. at ¶ 14 [redacted]).

The foregoing alone should be sufficient to foreclose plaintiff's argument that Lupin admitted infringement through its package insert. However, there is another roadblock for plaintiffs' infringement argument based on the package insert. Not only does Lupin's package insert report on tests conducted on a different product (Fortamet®), but the tests themselves are not those required by the patent for determining infringement.

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[14] Sec. 314.94(a)(8)(iv) also permits labeling to be modified "because of differences approved under a petition filed under § 314.93." Such a petition is called a "suitability petition," and seeks "permission to file an ANDA for a drug product that has one active ingredient in a combination product, or whose route of administration, dosage form or strength differs from that of the listed drug." 57 Fed. Reg. 17951-52 (April 28, 1992). A suitability petition is not available to make a change in labeling where, as here, there is no combination product and no difference in the route of administration, dosage form or strength. 57 Fed. Reg. 17957 (comment 20) (April 28, 1992).

The patent claim requires tests of a single dose, but the package insert table involves administration of multiple doses. The package insert refers to a reported $T_{max}$ for the "steady state," which by definition involves multiple doses, and also describes that the patients received doses once or twice a day for four weeks. This Court ruled, however, that "single dose" means "the amount of the drug administered to a human patient *at one time*." Markman Op. (D.I. 191) at 12 (emphasis added). Consistent with that ruling, the definition of single dose in the patent excludes the steady state, '866 patent at 7:60-62, and the patent defines "steady state" as being achieved "after repeated doses to dose of the formulation."[15] *Id.* at 7:57-59.

In sum, Lupin's labeling does not represent that a single dose of Lupin's product following dinner produces a $T_{max}$ of 6 hours, and thus does not trump the actual test on Lupin's product [redacted]. Plaintiff's argument to the contrary cannot stand after *Pliva*, and overlooks that the table in Lupin's package insert is reporting the result of a *multi-dose* test on the *Fortamet*® product, rather than a single dose test on Lupin's product.

**3. Asserted Claims 1, 3, 4, 5 and 25 Of The '866 Patent Are Invalid**

A patent claim must be novel and non-obvious in order to be valid. *See generally* 35 U.S.C. §§ 102, 103. "Taken together, the novelty and nonobviousness requirements express a congressional determination that the purposes behind the Patent Clause are best served by free

[15] The patent provides: "The term 'steady state' means that the blood plasma concentration curve for a given drug does not substantially fluctuate after repeated doses to dose of the formulation. *The term 'single dose' means that the human patient has received a single dose of the drug formulation and the drug plasma concentration has not achieved steady state.* The term 'multiple dose' means that the human patient has received at least two doses of the drug formulation in accordance with the dosing interval for that formulation (e.g., on a once-a-day basis). Patients who have received multiple doses of the controlled release formulations of the invention may or may not have attained steady state drug plasma levels, as the term multiple dose is defined herein." The '866 patent at 7:57-8:2. (emphasis added)

competition and exploitation of either that which is already available to the public, or that which may be readily discerned from publicly available material." *Bonito Boats Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 150 (1989).

The putative "invention" of the '866 patent was at least "readily discerned from publicly available material." *Id.* at 150. Prior art before the patent examiner, particularly *Cheng*, the published foreign counterpart of the '859 patent,[16] disclosed a mean $T_{max}$ as low as 8 hours. The examiner accepted the argument that the claims were allowable if the ceiling on the $T_{max}$ was 7 hours, giving a range of 5.5 to 7 hours. *See* Steiner Dec. ¶ 36. So plaintiffs stated in a paper filed in the PTO reporting on the interview with the examiner:

> During the Interview, the $T_{max}$ data presented in the Cheng, et al. reference was discussed in detail, and the Examiner's attention was directed to the discussion provided in applicants' responsive papers of February 2003 with respect to the $T_{max}$ information presented in the '859 patent. It was pointed out to the Examiner that the '859 patent was the U.S. priority application to the Cheng, et al. reference. The relationship of the claimed $T_{max}$ range of claim 1 (5.5 - 7.5 hours) when the dosage forms of the invention are administered after dinner was discussed with respect to providing the highest level of the drug in the blood at night (when gluconeogenesis is greatest; see the specification at pages 13-14). *The Examiner considered the closest prior art to teach a $T_{max}$ of 8 hours (the Cheng, et al. reference*). *The Examiner agreed that claim 5, which had an upper $T_{max}$ of 7.0 hours* and which value is directly supported by the working examples, *is patentably distinct over the Cheng, et al. reference*. The Examiner further agreed to consider the patentability of the broader range to 7.5 hours if applicants were to provide a working example of that value, as well.
>
> In view of the deadline for filing this response and in order to expedite the prosecution of this application to issuance, claim 1 has been cancelled by virtue of this amendment and claim 5 has been modified into independent form . . . .

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[16] Generally speaking, a publication by an inventor must be publicly available a year before the filing date of a patent in order to be considered prior art. The application that gave rise to the '866 patent was filed on Nov. 3, 2000. The '859 patent was not issued until August 8, 2000 (therefore, less than a year before the '866 patent's filing date), but the international version of the '859 patent, Cheng, WO 99/47125 was published on September 23, 1999. Thus the patent examiner used Cheng WO 99/47125 as prior art, but the substance of its disclosure is the same as that of the '859 patent, with which the Court is already familiar.

(Steiner Dec. Exh. L at AND 0000272) (emphasis added).

The claims were changed in accordance with this proposal and then ultimately allowed, but through one or more errors by the PTO, the ultimately allowed claims were not included in the patent as issued. Steiner Dec. at ¶¶ 12, 39, 42. In other words, none of the claims in the '866 patent as printed were ultimately allowed by the PTO. Steiner Dec. ¶¶ 12, 39, 42.

The Court's Markman Order equated "mean time to maximum plasma concentration" with "$T_{max.}$"[17] Especially with that construction, all of the asserted claims of the '866 patent are presumptively invalid as obvious from Cheng (WO 99/47125), the foreign counterpart of the '859 patent, in view of Timmins (WO 99/47128). Cheng and the '859 patent disclose every limitation of the asserted '866 claim except for the $T_{max}$ range of 5.5 to 7.5 hours following dinner.[18] Timmins discloses a controlled release metformin dosage form giving a $T_{max}$ of 4-8 hours following dinner. Expert Declaration of Kenneth R. Morris ("Morris Dec.") at ¶ 17.

During the prosecution of the '866 patent, and in an effort to overcome a rejection of the examiner, plaintiffs made an admission that is devastating to their case now. Plaintiffs told the patent examiner that "one skilled in the art would be able to manipulate the processes and formulations of the '859 by other methods to obtain the claimed pharmacokinetic parameters of

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[17] The Court's Markman Order equates the phrase "mean time to maximum plasma concentration" and "$T_{max}$." D.I. 192. The Court's Markman Opinion states that the parties agreed to the definition of "mean $T_{max}$." D.I. 191. Lupin respectfully points out that prior to the Markman hearing, the parties had agreed on the definition of "$T_{max}$"—shorthand for time to maximum plasma concentration—in the phrase "mean time to maximum plasma concentration," and had agreed on the definition of "mean," but had not agreed that "mean time to maximum plasma concentration" was always synonymous with "$T_{max}$" *See* D.I. 77-1 at 14. Nevertheless, the discussion in the text follows the Markman Order.

[18] The *in vitro* dissolution data claimed in claims 4 and 5 of the '866 patent are disclosed in the '859 patent at 8:38-44. The other limitations (controlled release metformin dosage form, passageway, membrane, etc.) are disclosed throughout the '859 patent. *See, e.g.,* the 859 Patent at 2:34-43.

the present invention by routine experimentation." Brauerman Dec. Exh. 9 (AND 0000236); Exh. E to Steiner Dec.

This concession leads directly to the presumptive invalidity of the asserted claims of the '866 patent, especially after the Supreme Court's 2007 groundbreaking *KSR* decision in the interim. *KSR Int'l Co. v. Teleflex, Inc.,* 550 U.S. 398, 418 (2007) ("If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.") Timmins discloses the desirability of a $T_{max}$ from 4-8 hours following dinner. Morris Dec. at ¶¶ 14, 19. The prior art $T_{max}$ range of 4-8 hours encompasses the claimed range of 5.5 to 7.5, making the claimed range presumptively obvious. "Where a claimed range overlaps with a range disclosed in the prior art, there is a presumption of obviousness." *Ormco Corp. v. Align Technology*, Inc., 463 F.3d 1299, 1311 (Fed. Cir. 2006).[19]

Both the '859 patent (Cheng) and Timmins were admittedly references cited to the patent examiner, and ordinarily one would apply the presumption that the examiner must have found a patentable distinction between the issued claims and the cited prior art. But not here, because in an odd twist noted above, the examiner did not ultimately allow the claims of the issued patent.

The claims that issued in the '866 patent were the wrong claims, as detailed in the accompanying declaration of Arthur Steiner, Esq., a former patent examiner with 40 years of

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[19] "The presumption can be rebutted if it can be shown that the prior art teaches away from the claimed range, or the claimed range produces new and unexpected results." *Id.* Plaintiffs make no such showing in their moving papers, nor can they. Timmins discloses the overlapping $T_{max}$ following dinner – thus teaching toward rather than away from the claimed range, and thus presumably achieving the same result on gluconeogenesis following dinner. Although plaintiffs argue that the "secondary consideration" of copying supports the non-obviousness of the claimed invention (Shionogi Mem. at 22 n. 16), it is well established that, in the generic drug context, "copying" is of virtually no weight in the obviousness inquiry. *See Santarus, Inc. v. ParPharm, Inc.,* 720 F. Supp. 2d 427, 458 (D. Del. 2009) ("[A] showing of copying is not compelling evidence of non-obviousness in Hatch-Waxman cases due to the nature of the ANDA process.")

experience with patent law. Steiner Dec., especially ¶¶ 12 *et seq*. The prosecution history of the '866 patent shows that, through PTO error, claim 1 with a $T_{max}$ range ceiling of "7.5 hours" was included in the patent, when in fact the examiner had rejected claim 1 as obvious with that maximum, and ultimately only approved claims with a $T_{max}$ ceiling of "7 hours" in the face of prior art disclosing, for example, a $T_{max}$ of 8 hours. Thus, plaintiffs cannot fairly point to a presumption of validity of the patent in response to Lupin's argument of obviousness. The rationale underlying the presumption of validity is that the PTO, in its expertise, has approved the patent claims,[20] but that did not happen here.

Especially without any presumption of validity, plaintiffs have not shown, and cannot show, how they can overcome Lupin's strong invalidity case, which demonstrates, *inter alia*, that it would have been obvious from prior art teaching a $T_{max}$ of 8 hours to make essentially the same dosage form with a $T_{max}$ of 7.5 hours (or below). All but one of the claims asserted against Lupin extend the $T_{max}$ value to 7.5 hours,[21] too close to the 8 hours of the prior art for the examiner to be willing to allow and thus presumptively too close for this Court to assume their validity.[22] For

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[20] *KSR Int'l Co.*, 550 U.S. at 426; *Microsoft Corp. v. i4i Ltd. P'ship*, __ U.S. ___, 131 S. Ct. 2238, 2249 (2011) (discussing *KSR).*

[21] The exception is Claim 3, which is very narrow and clearly not infringed by Lupin's product. Claim 3 reads: "The controlled release dosage form of claim 1, which provides a mean time to maximum plasma concentration ($T_{max}$) of metformin *at from* 5.5 to 7.0 hours after the administration of the dose." (emphasis added). The addition of the word "at" in the emphasized phrase was part of an amendment intended to overcome an examiner's rejection (Steiner Dec. Exh. E and ¶ 30; see Steiner ¶¶ 34, 36), and thus is presumed to be material. *See Warner-Jenkinson Co. v. Hilton Davis Chemical Co.,* 520 U.S. 17, 32 (1997) (" ... a lower limit of 6.0, by its mere inclusion, became a material *element* of the claim ...") (emphasis in original). While the language is not a model of clarity, the best reading of it would be that the $T_{max}$ encompasses the 1.5 hour period (5.5 to 7.0 hours), rather than merely requiring that the $T_{max}$ occur at some point during the 1.5 hour period. The plateau in $T_{max}$ profile for Day 14 in Figure 3 of the '866 patent illustrates this construction.

[22] What is now Claim 4 was not rejected by, but objected to, by the examiner, and while he indicated that the claim would be allowed if the applicants revised the claim to correct a

purposes of this motion, the claims improperly issued are the patent claims against which the validity challenge must be measured.[23] So measured against the *KSR* yardstick, the claims of the '866 patent are likely to be found invalid for obviousness.

### B. Plaintiffs Have Failed To Carry Their Burden Of Showing An Imminent Threat Of Irreparable Injury; Any Harm Would Be Compensable By Monetary Damages Or Is Too Speculative To Support Shionogi's Motion

[redacted]

Any harm to Shionogi is clearly quantifiable, and therefore not irreparable since Lupin is more than able to pay any damages that might be awarded. Shionogi itself prepared projections showing its anticipated sales and profits through March 2013; a comparison between these projections and what it actually sells is one approach to quantifying its damages. Shionogi even prepared projections for the impact on its sales and profits in the event a generic Fortamet® product entered the market, showing again that the effect of a generic launch can be quantified.

[redacted]

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deficiency, Plaintiffs never reworked the claim. Steiner Dec. ¶ 31. This Court is foreclosed from rewriting the claim for the patentee. *Group One, Ltd. v. Hallmark Cards, Inc.*, 407 F.3d 1297, 1303 (Fed. Cir. 2005).

[23] *See also Novo Industries, L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1356 (Fed. Cir. 2003) ("For causes of action that arise before the correction becomes effective, the patent must be considered without the benefit of the certificate of correction"). The Federal Circuit in *Novo* said that a district court lacks statutory authority to correct a clerical error not apparent on the face of the patent. *Id.* at 1357. There is no indication that plaintiffs have made any effort to obtain a certificate of correction to rectify this problem with the '866 patent. Steiner Dec. at ¶ 40.

[redacted]

**1. Legal Standard**

As with the likelihood of success factor, the recent opinion in *King Pharms.,* 2010 WL 1957640, denying a preliminary injunction against a generic drug defendant, summarizes the applicable legal standard. First, "[p]laintiffs must provide a 'clear showing' that it will suffer irreparable harm in the absence of injunctive relief." *King Pharms.,* 2010 WL 1957640, at *5 (citing *Nutrition 21 v. United States,* 930 F.2d 867, 870-71 (Fed. Cir. 1991) and *Winter*, 550 U.S. at 20-24). Second, "[i]rreparable harm must be established as a separate element, independent of any showing of likelihood of success; irreparable harm can no longer be presumed." *Id.* Third, "courts have routinely decided that market share and price erosion do not amount to irreparable harm." *Id.* (citing *Nutrition 21*, 930 F.2d at 871 (Fed. Cir. 1991); *Eli Lilly v. American Cynamid Co.*, 82 F.3d 1568, 1578 (Fed. Cir. 1996) ("Such a rule would convert the 'extraordinary' relief of a preliminary injunction into a standard remedy available whenever the plaintiff has shown a likelihood of success on the merits.")).

Further, "establishing a risk of irreparable harm is not enough. A plaintiff has the burden of proving a 'clear showing of immediate irreparable injury'" absent injunctive relief. *Hoxworth v. Blinder, Robinson & Co. Inc.*, 903 F.2d 186, 205 (3d Cir. 1990) (quoting *ECRI v. McGraw–Hill, Inc.*, 809 F.2d 223, 225 (3d Cir. 1987)). Failure to establish irreparable injury automatically results in denial of a preliminary injunction. *Instant Air Freight Co. v. C.F. Air Freight, Inc.*, 882 F.2d 797, 800 (3d Cir. 1989); *see also NutraSweet Co. v. Vit-Mar Enterprises, Inc.*, 176 F.3d 151, 153 (3rd Cir. 1999).

**2. Claimed Loss Of Revenue, Market Share And Jobs Is Exaggerated And Compensable With Money Damages**

Shionogi's first argument for irreparable injury is that it will lose market share to a generic entry, because most states require substitution of the less expensive generic drug in place of the costly brand product. (Shionogi Mem. at 23). If loss of market share were sufficient to show irreparable injury, then every generic product would be enjoined at the request of the brand manufacturer. *See e.g., Abbott Labs. v. Andrx Pharms., Inc.*, 452 F.3d 1331, 1348 (Fed.Cir. 2006) ("[I]f this court were to accept a patentee's argu[ments] that, apart from the presumption, its potential lost sales alone demonstrate manifest irreparable harm, acceptance of that position would require a finding of irreparable harm to every manufacturer/patentee, regardless of circumstances." (internal quotations omitted)).

[redacted] Such allegations are wholly insufficient to direct the court to find irreparable harm. *See, e.g., Eli Lilly & Co. v. Am. Cyanamid Co.*, 82 F.3d 1568, 1578 (Fed. Cir. 1996) ("If a claim of lost opportunity to conduct research were sufficient to compel a finding of irreparable harm, it is hard to imagine any manufacturer with a research and development

program that could not make the same claim and thus be equally entitled to preliminary injunctive relief."); *Novartis Corp. v. Teva Pharms. USA, Inc.,* Civ. Nos. 04-4473, 2007 WL 1695689, at * 28 (D.N.J. June 11, 2007) (citing *Eli Lilly* and finding that "any potential or attenuated damage to Novartis's ability to fund R & D does not compel entitlement to a preliminary injunction").

[redacted] This falls far short of the extremely demanding standard required to render injury to market share irreparable. *See Graceway Pharms., LLC v. Perrigo Co.,* 722 F. Supp. 2d 566, 578 (D.N.J. 2010).

Shionogi surprisingly points to the Plavix at-risk generic launch as illustrative precedent. Shionogi argues that some generic companies have "flooded" the market with almost one year's supply when they launched, [redacted]

The Plavix experience to which Shionogi alludes also shows that even a launch of a large amount of generic product does not produce irreparable harm. Within a year of Apotex's launch, the brand company had recovered its entire market share and the sales for the brand product had

increased. The effect of the generic launch had vanished from the market. Gleason/Hofmann at 52.

### 3. Claimed Loss Of Formulary Status Is Merely Loss Of Market Share Which Is Compensable With Money Damages

Shionogi's argument that it will lose formulary status is nothing more than an explanation for its projected loss of market share. Formulary status shows what the co-pay cost will be of the drug; co-pays for generic drugs are lower than co-pays for brand products, especially where there is a generic alternative to the brand. Shionogi's argument, therefore, is that it will lose sales because its product will cost more is the same argument as it made with respect to the lower generic price. Gleason/Hofmann Dec. at 55-56.

Shionogi's assertions also are not supported by its own facts. Fortamet® already is a Tier III drug for most formularies; [redacted] Its speculation that it might be removed from the formulary entirely is rebutted by the fact that both of the other branded metformin products (Glucophage and GlucophageXR) remain on the formularies despite the availability of generic versions. Gleason/Hofmann Dec. at n. 79.

In any event, damage stemming from the loss of a formulary position is compensable by monetary damages. *See AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579, 610 (D.N.J. 2009) *supplemented*, 623 F. Supp. 2d 615 (D.N.J. 2009), *aff'd*, 633 F.3d 1042 (Fed. Cir. 2010) *and aff'd*, 633 F.3d 1042 (Fed. Cir. 2010) ("damages from loss of formulary positions are reasonably calculable"; in a case concerning the threat of a generic moving a brand from Tier 2 to Tier 3, the "loss of tier status will translate into sales losses that should be quantifiable... Thus it seems these damages are reasonably calculable and compensable."). Accordingly, Shionogi has no basis here to claim irreparable injury due to loss of formulary tier positioning.

**4. Entry Of Authorized Generic Proves That Enjoining Lupin Will Have No Effect On Putative Harm To Shionogi**

Lupin's launch of its generic product gives Watson/Andrx the right to launch an authorized generic. [redacted], all of the harm which Shionogi claims has befallen it as a result of generic competition, will continue even if Lupin is enjoined, because the authorized generic will create the same problems. Here, Shionogi affirmatively acknowledges that the injury it asserts it will suffer will occur absent injunctive relief against Lupin (*cf*. *Hoxworth*, 903 F.2d at 205) and that an injunction will not cure the alleged injury.

**5. Claimed Loss Of Goodwill Is Entirely Speculative And Contrary To Common Sense**

Working down its checklist of factors which courts have found could constitute irreparable injury with a proper showing in appropriate circumstances, Shionogi speculates without support or evidence that it faces a number of non-economic harms from the presence of generic competition. Even if these supposed harms would support an injunction – and many courts have found that they do not – in the absence of proof, unsupported claims and speculations cannot support the exceptional relief which Shionogi here requests. *E.g.*, *Altana Pharma AG.*, 566 F.3d at 1005 (affirming district court denial of injunction, despite allegations of "irreversible price erosion, substantial loss of profits, decrease in market share, inability to service debts, employee layoffs, and loss of research opportunities")[24]

[24] *See, e.g.*, *Novartis Pharm. Corp. v. Teva Pharm., USA, Inc.*, C.A. No. 05-CV-1887, 2007 WL 2669338, at *15 (D.N.J. Sept. 6, 2007) (no irreparable harm found; claims that customers will become accustomed to generic drug prices, and will harbor ill-will if generic later becomes unavailable were "purely speculative"); *Graceway Pharm., LLC v. Perrigo Co*., 722 F. Supp. 2d at 579 ("lost jobs, price erosion, market share, and *business reputation* are compensable by money damages and readily calculable as Aldara is a mature product" (emphasis added)).. *Sanofi-Aventis Deutschland GmbH v. Glenmark Pharms. Inc.*, USA, Civ. Action No. 07-CV-

[redacted] In addition, Shionogi argues elsewhere that it will lose goodwill because the customers "may" blame it for removing a lower-priced generic drug from the market. It cannot have it both ways: either the customers will know that the lower-priced product is not Shionogi's and not blame Shionogi for any perceived differences in quality, or they will think that the product is Shionogi's and will give Shionogi credit for the lower price. The inconsistency in Shionogi's assertions highlights the complete lack of evidentiary or factual support for their claims.

Shionogi continues that customers "may" blame Shionogi for price fluctuations, although it seems unlikely that there are many individual customers or any retail customers who are not aware of the interplay between generic and brand products. *See* Gleason/Hofmann Dec. at 40-41. In addition, [redacted] the metformin extended release market is highly genericized already. Any customer who is very sensitive to the size of the co-pay would have switched to one of the generic metformin extended release products, so it seems unlikely that they would resent Shionogi for selling a brand product.

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5855 (DMC), 2010 WL 2428561 at *17 (D.N.J. June 9, 2010) (denying injunction and finding plaintiff's claim of loss of goodwill due to a generic entering the market is "too speculative" to consider for irreparable harm analysis); *Quad/Tech, Inc. v. Q.I. Press Controls B.V.*, 701 F. Supp. 2d 644, 656 (E.D. Pa. 2010) (no proof of irreparable harm where plaintiff only supported claims of eroded customer expectations via "conclusory, speculative" declarations), *aff'd*, 413 F. App'x 278 (Fed. Cir. 2011).

[redacted]

**6. Shionogi's Unexplained Delay In Seeking Injunctive Relief and Failure To Take Any Steps To Protect Itself From A Launch Of Which It Was Warned Shows That Any Harm Is Neither Imminent Nor Irreparable**

A telling fact is that plaintiffs took no steps to protect themselves from a commercial launch that they anticipated, if not from the beginning of the litigation, certainly for at least the last three months. Shionogi's own conduct in failing to protect its rights demonstrates a lack of immediate irreparable harm. *E.g.*, *Novartis Corp. v. Teva Pharmaceuticals USA, Inc.*, Civ. Nos. 04-4473 HAA ES, 2007 WL 1695689, at * 30 (D.N.J. June 11, 2007) (finding unreasonable delay because plaintiff's motion "was filed more than *a month* after the statutory 30-month stay expired)" (emphasis added).

Even though businesses routinely (and appropriately) keep their competitive plans secret,[25] Lupin had not been subtle about considering a launch. [redacted] Lupin's Chief Financial Officer publicly announced that Lupin intended to launch its generic metformin product in a widely-covered statement that was published in the Wall

[25] "It is an ordinary and acceptable business practice to keep one's new developments a secret." *Berkey Photo, Inc. v. Eastman Kodak Co.,* 603 F.2d 263, 281 (2d Cir. 1979), *cert. denied,* 444 U.S. 1093 (1980).

Street Journal and elsewhere two days before the launch took place. Brauerman Dec. Exh. 9)[26] The same newspaper had reported a few months earlier that Lupin would launch "this year." Brauerman Dec. Exh. 8). Shionogi concedes that it knew on September 30 from market information that Lupin had launched its product (Shionogi Mem. at 9), yet it still delayed before taking any action. As numerous courts have held, Shionogi's delay suggests the absence of the required element of immediate irreparable harm. *See, e.g., Hybritech Inc. v. Abbott Labs.,* 849 F.2d 1446, 1457 (Fed.Cir. 1988) (period of delay may be a significant factor in irreparable harm analysis).

Further, under the agreement between Shionogi and Watson's predecessors, the mere fact of Lupin's launch means that regardless of whether Lupin is enjoined, Watson's approved generic product is free to enter the market; [redacted] Gleason/Hofmann Dec. ¶¶ 48-50. While Shionogi claims that it will suffer a panoply of irreparable harms due to Lupin's launch, Watson's entry into the market with its generic would create the same results, and Shionogi does not seek to enjoin Watson's entry. [redacted]

[26] [redacted]

Shionogi of course has been aware of Watson's contractual rights since well before this litigation began. *See Pharmacia Corp. v. Alcon Labs., Inc.,* 201 F.Supp.2d 335, 383 (D.N.J. 2002) ("[s]uch a delay – one full year – knocks the bottom out of any claim of immediate and irreparable harm.") Thus, even though it might not have known precisely when Lupin would launch, Shionogi has known all along that any generic launch would give Watson the right to enter the market with its own generic, bringing with it all of the alleged harm that Shionogi claims it will suffer due to having to compete with a generic metformin. Yet Shionogi sat on its rights and never attempted to enjoin Lupin's launch until after it occurred.

### C. Shionogi Has Failed To Carry Its Burdens On The Balance Of Hardships And Public Interest Factors

#### 1. The Balance Of Hardships Favors Lupin

Although Shionogi's failure to establish either likelihood of success on the merits or irreparable injury should lead to a denial of its motion for a preliminary injunction, Shionogi also has failed to show that the balance of hardships tilts in its favor. "When evaluating the balance of hardships, a 'court must balance the harm that will occur to the moving party from the denial of the preliminary injunction with the harm that the nonmoving party will incur if the injunction is granted.'" *Novartis Corp.,* 2007 WL 1695689, at *28 (quoting *Hybritech, Inc. v. Abbott Labs.,* 849 F.2d 1446, 1457 (Fed. Cir. 1988)).

The facts presented here are different from most pharmaceutical preliminary injunction situations and those in the cases cited by Shionogi. The Fortamet® market is in steady and irreversible decline, and has been for some time. [redacted]

[redacted] If Lupin had waited until the litigation was concluded, there may not have been a Fortamet® market for it to enter. These factors distinguish this case from those cited by Shionogi finding that the hardship to the generic is merely "time-shifting" the anticipated profits. *Albany Molecular Research, Inc. v. Dr. Reddy's Labs., Ltd.*, 2010 WL 2516465, at * 11 (D.N.J. June 14, 2010).

Lupin will suffer serious, and in some instances irreparable, harm if the preliminary injunction is granted. As the first generic company to file an ANDA, Lupin is entitled to a 180-day exclusivity period when it is the only non-authorized generic on the market. Hoffman Dec. ¶ 6. This exclusivity period is meant to encourage generic companies to develop generic products and to reward their investment and risk for doing so. Since Lupin has begun to market, its 180 day exclusivity period has started to run, and once started it does not stop. This is a lost opportunity that cannot be regained later, once Lupin is successful at trial. Hoffman Dec. ¶¶ 7-11. *See In re Cyclobenzaprine Hydrochloride Extended Release Capsule Patent Litigation,* Civ. No. 09-MD-2118, 2011 U.S. Dist. LEXIS 54062, at * 9-10 (D.Del. 2011) (recognizing loss of 180-day exclusivity as "a legitimate concern," but finding in that case it is outweighed by irreparable harm to brand). Similarly, Lupin is entitled to realize the benefit of having filed its ANDA one year before the next generic competitor, so that even after its 180-day exclusivity period expired, it still would enjoy some months before the mandatory 30-month stay expires for the Mylan defendants.[27]

[27] This is not a situation as in *Research Foundation of SUNY v. Mylan Pharm.,* 723 F. Supp. 2d at 661-62 (D. Del. 2010), where the court discounted the time after the 180-days when the generic would have been alone on the market because of a statutory quirk. Here, Lupin's additional time on the market as the only generic is the result not of "unusual circumstances" but something to which it has "a statutory, or equitable, entitlement" as a result of the timing of its ANDA filing. *Id.*

The damage to Lupin's reputation and relationship with its customers is another harm to Lupin, this one irreparable. Lupin's customers expect it to honor its contracts, and a company which cannot honor its commitments for one product will have more difficulty selling other products. Hoffman Dec. at ¶ 22. This damage to reputation cannot be quantified and cannot be cured if the injunction is found a year from now to have been improvidently granted. *Id.*

Likewise, Lupin is ready and willing to supply the 500mg tablet market, [redacted] it is in danger of disappearing, and once gone, would be too small to resuscitate. Hoffman Dec. at ¶ 25. Shionogi cannot claim a hardship by Lupin being permitted to sell to a market it has ignored.

**2. The Public Interest Favors Greater Availability Of Generic Drugs**

Congress has made the policy judgment that the public interest is furthered by greater availability of generic drugs. *In re Barr Labs, Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991), *cert. denied*, 502 U.S. 906 (1991) ("Congress sought to get generic drugs into the hands of patients at reasonable prices – fast"); *Mylan Pharms., Inc. v. Thompson*, 268 F.3d 1323, 1326 (Fed. Cir. 2001). In the Hatch-Waxman Act, Congress balanced that policy against the interest in enforcing valid patent rights by setting a limited amount of time (generally 30 months) for resolving patent-related issues that arise in connection with the generic drug application, before

the FDA is free to grant approval for marketing the generic drug. *See* 21 U.S.C. § 355(j)(5)(B)(iii); *Mylan Pharm.,* 268 F.3d at 1325-26.

In the present case, Shionogi asks for the extraordinary relief of a preliminary injunction and the "drastic remedy" of a recall based on patent claims that it knows or should have known were not ultimately allowed. Especially in light of the fact that the PTO had once before for this patent application approved the wrong claims for issuance (*e.g.* claims that had been earlier cancelled; s*ee* Steiner Dec. ¶ 34), Shionogi had a duty to check for errors: "it does not seem to us to be asking too much to expect a patentee to check a patent when it is issued in order to determine whether it contains any errors that require the issuance of a certificate of correction." *Southwest Software, Inc. v. Harlequin, Inc.,* 226 F.3d 1280, 1296 (Fed. Cir. 2000).

Under the circumstances, there is no countervailing public interest to offset Congress' policy judgment that, in the absence of a final determination that the patent is valid and infringed, 30 months is long enough for the public to wait for generic competition. Nor does the public interest favor those who, like Shionogi, sit on their rights, and then – after the fact – try to delay the generic competition Congress has sought. Lupin played by the rules: it waited 30 months, obtained final FDA approval, and has now begun bringing to consumers the generic drugs that Congress wants the public to have. There has been no final determination that either patent is valid and infringed and, as discussed above, the likelihood of such a result is remote. The public interest thus favors denial of a preliminary injunction.

**D. Shionogi Cannot Meet The Heavy Burden Required to Order A Recall**

At the end of its preliminary injunction brief, Shionogi appends a passing request for a recall of all the generic metformin that Lupin has sold into the market. A request for a recall is a request for a mandatory injunction, because it seeks to change the *status quo* and not preserve it. Accordingly, a recall is a truly extraordinary remedy, and Shionogi bears a heavy burden.

Shionogi's argument seems little more than an afterthought and does not meet this demanding standard.[28]

A preliminary injunction is a "drastic and extraordinary remedy that is not to be routinely granted." *Novartis Corp. v. Watson Labs*., 2007 U.S. Dist. Lexis 42163, at * 9-10 (D.N.J. 2007) "*see also United States v. Price,* 688 F.2d 204, 212 (3d Cir. 1982).[29] "A mandatory injunction is said to alter the *status quo* by commanding some positive act . . . [and] should issue only upon a clear showing that the moving party is entitled to the relief requested, or where extreme or very serious damage will result from a denial of preliminary relief." *Advanced Oral Technologies, L.L.C. v. Nutres Research, Inc.*, 2011 WL 13881, at *2 (D.N.J. Jan. 3, 2011). Here, the recall order seeks to alter the *status quo*, because the last uncontested state before Shionogi moved for injunctive relief was after Lupin had already shipped its product. Indeed, as described above at length, despite numerous warnings and notices that Lupin would launch, Shionogi chose to wait until well after Lupin's launch before filing its motion. *See Novartis ,*2007 U.S. Dist. LEXIS 42163 at *98-99.

Shionogi cannot meet this heavy burden; indeed, it does not even try. Shionogi offers nothing – no evidence, and only token lawyer argument – in support of its specific and additional request for a recall.

By contrast, Lupin will suffer considerable and irreparable harm if it is ordered to undertake a recall. A recall would be onerous, complicated and expensive. Lupin would suffer

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[28] Lupin reserves its rights to seek leave to file a sur-reply should Shionogi attempt to offer arguments or evidence on the recall issue for the first time in its reply brief.

[29] The power to issue a preliminary injunction, especially a mandatory one [such as a recall order], should be sparingly exercised." *Oral Research Labs., Inc. v. L. Perrigo Co.*, 1988 WL 123501, at * 2 (Fed. Cir. Nov. 21, 1988) (bracketed phrase in original) (unpublished) (denying recall request in the context of alleged trade dress infringement).

considerable harm to its goodwill, reputation and its relationships with distributors and retailers if a recall were ordered, for the simple fact that customers do not like to do business with a company that recalls its products. And even if the recall were court-ordered, customers and end-users may speculate that the recall was due to health and safety reasons. Moreover, unlike a product recall in a non-regulated industry, any recall ordered here would have to be carried out through and with the direction of the Food & Drug Administration. This additional complication and oversight will require considerably more time and effort. Implementing the recall would take three to four months at a minimum, would take up thousands of hours of labor, and would cost millions of dollars. Distributors or retailers may not agree to return the products, which could require additional work and further involvement of the Court. *See generally* Hoffman Dec. ¶¶ 26-30.

**Amount of a Bond Pursuant to Fed. R. Civ. P. 65(c)**

For the reasons set forth above, Shionogi is not entitled to a preliminary injunction and so the Court need not reach this issue. [redacted]

## V. CONCLUSION

To be entitled to a preliminary injunction, plaintiffs must demonstrate both a likelihood of success on the merits and the threat of irreparable injury if the relief is not granted. Here they have demonstrated neither. Moreover, Lupin would be hurt more by an improvident granting of an injunction than plaintiffs will be harmed by an improvident denial, and the public interest favors denial of the extraordinary relief sought by plaintiffs. In short, plaintiffs establish none of

the four factors relevant to a motion for preliminary injunction, and provide no basis for a recall, and thus the motion should be denied in its entirety.

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